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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
TUNG, J	
ART UNIT	**PAPER NUMBER**
1656	18

DATE MAILED: 10/11/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/076,115	Gruber et al
Examiner	**Group Art Unit**
Joyce Tung	1656

☒ Responsive to communication(s) filed on *Aug 28, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1, 2, 6, 12, 16-20, 22, 25, 28, 29, 31, 32, and 41-43* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 2, 6, 12, 16-20, 22, 25, 28, 29, 31, 32, and 41-43* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 8/28/2000 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/076,115 is acceptable and a CPA has been established. An action on the CPA follows.

2. Regarding the rejection of claims 1-2, 6, 12, 16-20, 22, 25, 28,29, 31-32 and 41-43 under 103(a) over Burmer. The response argues the adaptors of Burmer are not contained on primers used for synthesis of nucleic acid molecule and instead, Burmer describes ligating double-stranded adaptors to nucleic acid fragment and Burmer therefore is seriously deficient as a primary reference. Although Burmer does not disclose using a primer-adapter nucleic acid molecule to amplify the target nucleic acid, Burmer does disclose that the fragmented nucleic acid is ligated to an adapter with a restriction site, and the adapter may optionally contain a ligand binding end and Burmer does also disclose that the primers used for second nucleic acid fragment amplification contains a ligand binding end and a sequence complementary to the adapters (See column 2, lines 39-48) which comprises a restriction site. Based upon the disclosure of Burmer, an artisan of ordinary skill in the art at the time of the instant invention would have made a primer-adapter as claimed comprising ligands and restriction cleavage sites. Therefore the rejection of claims 1-2, 6, 12, 16-20, 22, 25, 28,29 and 31-32 is maintained. The rejection of claims 41-43 are withdrawn.

3. Claims 1, 2, 6, 12, 16-20, 22, 25, 28, 29, and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burmer (5,726,022) in view of Carninci et al. (Genomics, 1996, Vol. 37, pg. 327-336).

Burmer discloses a method to isolate nucleic acid sequences. The method involves using an adaptor which includes a restriction site and a ligand binding end ligated to the nucleic acid fragment of a first and second nucleic acid samples to provide the nucleic acid complementary to a primer for amplification (see column 4, lines 16-25). If the fragment of the second nucleic acid samples are amplified, the primers used contain a ligand binding end (see column 4, lines 26-30). The isolation step is done by first removing the adaptors by restriction enzyme, capturing the nucleic acid containing the ligand and then the nucleic acid that were not captured is isolated (see column 2, lines 56-59). The ligand includes hapten (see column 7, line 4). The amplification is done by PCR, LCR and TAS (see column 8, lines 47-52). The solid support is described in column 7, lines 37-48.

Burmer does not disclose using a primer which has a restriction enzyme recognition site incorporated into a nucleic acid sequence via amplification.

Carninci et al. disclose a method for efficiently constructing high-content full-length cDNA libraries. The method involves using a primer inserted with restriction sites, the restriction sites are incorporated into cDNA by PCR with ExTaq DNA polymerase and the amplified nucleic acid is cleaved by the restriction enzyme (see pg. 329, column 1-2, the fourth and fifth paragraph).

The teachings of Burmer and Carninci et al. suggest instant claims 1, 2, 6, 12, 16-20, 22, 25, 28, 29, 31 and 32 in which the method is used for making or isolating a nucleic acid comprising mixing a DNA template with polymerase and a primer-adapter nucleic acid molecule containing a ligand and restriction site to produce a first nucleic acid molecule. The polymerase is described in instant claim 6. The method also involves making a second nucleic acid molecule complementary to the first nucleic acid molecule in which the steps are the same as for making the first nucleic acid molecule. The ligand binds to haptens bound to a solid support forming a nucleic acid ligand-hapten complex and the nucleic acid molecule is isolated by cleaving from the complex at the cleavage sites.

One of ordinary skill in the art at the time of the instant invention would have been motivated to combine the references of Burmer and Carninci et al. for a reasonable expectation of success because Burmer indicates that the method provides simple and inexpensive means for isolating a nucleic acid (see column 2, lines 24-25) since the method uses a ligated adaptor containing a restriction site and ligand which allows molecules to be rescued from both the captured population (see column 1, 59-64) and the method also involves a ligand binding primer for amplifying a nucleic acid fragment. The isolation is done by cleaving the restriction site and the nucleic acids which are not captured are isolated. These features of the method simplify the method. Carninci et al. teach using a primer inserted with restriction sites, the restriction sites are incorporated into an amplified nucleic acid via amplification and the amplified nucleic acid can be cleaved by a restriction enzyme. Therefore, an artisan of ordinary skill would have combined

the references by using a primer containing a restriction site and a ligand, and the restriction site and ligand are incorporated into a target nucleic acid by amplification reaction which have been taught in the reference above for making or isolating a nucleic acid sequence as claimed in instant claims. This would have even further simplified the steps by excluding the ligation step in which the adaptor is ligated to a target nucleic acid as taught by Burmer. It would have been prima facie obvious to carry out the method as claimed.

Claim Rejections - 35 U.S.C. § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

5. Claims 41-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Burmer (5,726,022).

Burmer et al. disclose the kit to perform the method as set forth in section above and that the kit has combinations of reagents and is useful in the methods in a separate container (See column 9, lines 20-34). This inherits that the kit has primers, enzymes and solid support to fulfil the method.

The teachings of Burmer et al. anticipate the limitations of instant claims 41-43. Instant claims 41-43 are drawn to a kit for the production of nucleic acid molecule comprising one or more containers in which a first container has a primer-adapter, an additional container has polymerase or reverse transcriptase and a third container has a solid support.

Claim Rejections - 35 U.S.C. § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 6, 20 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 6 is vague and indefinite because of the language "mutants and variants thereof that are substantially reduced in RNAse H activity". It is unclear what is the mete and bounds for the mutants and variants to reduce RNAse H activity. It is also unclear what is the metes and bounds to substantially reduce RNAse H activity. It is suggested to clarify uncertainty.

b. Claims 20 and 32 are vague and indefinite because it is unclear how said nucleic acid is isolated by cleavage of one or more of said cleavage sites.

8. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached at (703) 308-1152.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1656 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

October 5, 2000

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

10/8/00